

### REMARKS/ARGUMENTS

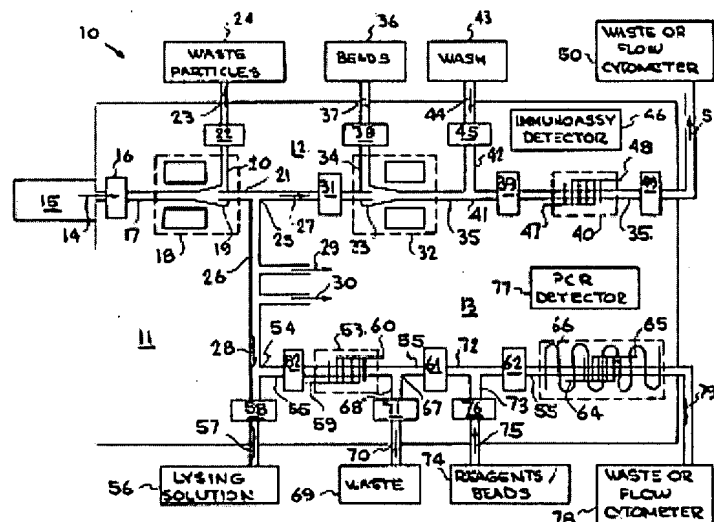
The Office Action mailed March 27, 2007 has been carefully reviewed. Reconsideration of this application, as amended and in view of the following remarks, is respectfully requested. The application as filed contained claims 1-50. Claims 41-50 are withdrawn in response to a restriction requirement. Claims 6-11, 13-14, 17-18, 20-26, 28, and 30 have been cancelled. The claims presented for examination are: claims 1-5, 12, 15-16, 19, 27, 29, and 31-40.

#### 35 U.S.C. §103 Rejection – Miles et al In View of Casey et al

In numbered paragraphs 6-17 of the Office Action mailed March 27, 2007, claims 1-4, 8, 9, 10-13, 27, 29, 31-35 and 40 were rejected under 35 U.S.C. §103(a) as being unpatentable over the Miles et al reference (US 6,576,459) in view of the Casey et al reference (US 2002/0187470).

#### The Miles et al Reference

The Miles et al reference is United States Patent No. 6,576,459 for a sample preparation and detection device for infectious agents illustrated in the figure and portion of specification of the patent reproduced below.



"The sample preparation and detection device comprises a system or device generally indicated at 10 located on a single compact, field-portable microchip 11 and includes an immunoassay section 12 and a PCR assay section 13. Sample containing pathogenic particles indicated by arrow 14 is moved from a collector or other source 15 by an MHD pump 16 through a microchannel 17 into an ultrasonic fractionation or filtering assembly generally indicated at 18 and which is sensitive to density and size differences between particles. Microchannel 17 terminates in a separator 19 with microchannels 20 and 21 extending from separator 19. Microchannel 20 is directed through a MHD pump 22 and carries large particles and dense particles indicated by arrow 23, which are transferred to waste as indicated at 24. Microchannel 21 includes a function 25 from which extends a microchannel 26, with microchannel 21 supplying sample to immunoassay section 12 as indicated by arrow 27 and microchannel 26 supplying sample to PCR assay section 13 for DNA analysis, as indicated by arrow 28."

#### The Casey et al Reference

The Casey et al reference is United States Published Patent Application No. 2002/0187470 disclosing methods for rapid detection of single nucleotide polymorphisms (SNPs) in a nucleic acid sample. For example, the Casey et al reference discloses the following method:

"a method of determining a selected nucleotide polymorphism in genomic DNA treated to reduce viscosity comprising (a) performing an amplification of the genomic DNA using a first nucleic acid primer comprising a region complementary to a section of one strand of the nucleic acid that is 5' of the selected nucleotide, and a second nucleic acid primer complementary to a section of the opposite strand of the nucleic acid downstream of the selected

nucleotide, under conditions for specific amplification of the region of the selected nucleotide between the two primers, to form a PCR product; (b) contacting the PCR product with a first nucleic acid linked at its 5' end to a detectably tagged mobile solid support, wherein the first nucleic acid comprises a region complementary to a section of one strand of the PCR product that is directly 5' of and adjacent to the selected nucleotide, under hybridization conditions to form a hybridization product; (c) performing a primer extension reaction with the hybridization product and a detectably labeled, identified chain-terminating nucleotide under conditions for primer extension; (d) detecting the presence or absence of a label incorporated into the hybridization product, the presence of a label indicating the incorporation of the labeled chain-terminating nucleotide into the hybridization product, and the identity of the incorporated labeled chain-terminating nucleotide indicating the identity of the nucleotide complementary to the selected nucleotide; and (e) comparing the identity of the selected nucleotide with a non-polymorphic nucleotide, a different identity of the selected nucleotide from that of the non-polymorphic nucleotide indicating a polymorphism of that selected nucleotide."

#### **Applicants' Response to Rejection Miles et al In View of Casey et al**

Applicants have amended the single independent claim, claim 1; therefore all of the claims presented for examination have effectively been amended.

Applicants believe Applicants believe that amended independent claim 1 and the dependent rejected claims are patentable and that the Miles et al and Casey et al references do not support a 35 U.S.C. §103(a) rejection.

The Examiner bears the initial burden of factually supporting a *prima facie* conclusion of obviousness. To establish a *prima facie* case of obviousness, three basic criteria must be met. First, there must be some suggestion or motivation, either in the references themselves or in the knowledge generally available to one of ordinary skill in the art, to modify the reference or to combine reference teachings. Second, there must be a reasonable expectation of success. Finally, the prior art reference (or references when combined) must teach or suggest all the claim limitations. The teaching or suggestion to make the claimed combination

and the reasonable expectation of success must both be found in the prior art, and not based on applicant's disclosure. *In re Vaeck*, 947 F.2d 488, 20 USPQ2d 1438 (Fed. Cir. 1991).

No Suggestion or Motivation to Combine Miles et al and Casey et al

The first criteria for supporting a *prima facie* conclusion of obviousness is: there must be some suggestion or motivation, either in the references themselves or in the knowledge generally available to one of ordinary skill in the art, to modify the reference or to combine reference teachings.

There is no suggestion or motivation to combine the Miles et al field-portable microchip sample preparation and detection device with the Casey et al methods for rapid detection of single nucleotide polymorphisms in a nucleic acid sample. There is no explanation of how or why the Miles et al microchip device would or could be combined with the Casey et al methods. Since there is no suggestion or motivation to combine the references Examiner has not factually supported a *prima facie* case of obviousness and the rejection should be withdrawn.

No Reasonable Expectation of Success

The second criteria for supporting a *prima facie* conclusion of obviousness is there must be a reasonable expectation of success. A combination of the Miles et al field-portable microchip sample preparation and detection device with the Casey et al methods for rapid detection of single nucleotide polymorphisms in a nucleic acid sample would not have a reasonable expectation of success. Casey et al shows methods and those methods could not be successfully implemented on the Miles et al microchip device. Since the combination would not have a reasonable expectation of success the Examiner has not factually supported a *prima facie* case of obviousness and the rejection should be withdrawn.

### References Do Not Teach or Suggest All the Claim Limitations

The Third criteria for supporting a *prima facie* conclusion of obviousness is the prior art reference (or references when combined) must teach or suggest all the claim limitations. In assessing any *prima facie* conclusion of obviousness the guidance of the Supreme Court in *Graham v. John Deere Co.*, 383 U.S. 1, 148 USPQ 459 (1966) is used. *Graham v. John Deere Co.* requires determining “the scope and content of the prior art,” ascertaining “the differences between the prior art and the claims at issue,” and resolving “the level of ordinary skill in the pertinent art.”

There are many differences between the Miles et al and Casey et al references and Applicants’ claimed invention. For example, Applicants’ claim limitations identified below are missing from the Miles et al and Casey et al references.

The Miles et al and Casey et al references do not show Applicants’ claim limitation, “a collector for gathering said air being monitored, said collector separating selected potential bioagent particles from said air (Claim 1).”

The Miles et al and Casey et al references do not show Applicants’ claim limitation, “a wetted wall sample preparer for preparing a sample of said selected potential bioagent particles, said wetted wall sample preparer operatively connected to said collector for collecting and preparing said sample from said air gathered by said collector, wherein said wetted wall sample preparer includes a wetted wall cyclone collector that concentrates said selected potential bioagent particles in a liquid and a unit for adding optically encoded microbeads imbedded with precise ratios of red and orange fluorescent dyes yielding an array of beads having a unique spectral address and each bead coated with capture antibodies specific for a given antigen to said liquid and said selected potential bioagent particles (Claim 1).”

The Miles et al and Casey et al references do not show Applicants' claim limitation, "a detector for detecting said bioagents in said sample, said detector operatively connected to said wetted wall sample preparer wherein said detector utilizes said optically encoded microbeads and wherein said detector includes a flow cytometer for analyzing said optically encoded microbeads that are imbedded with precise ratios of red and orange fluorescent dyes yielding an array of beads having a unique spectral address and each bead coated with capture antibodies specific for a given antigen with a laser unit for individually interrogating said optically encoded microbeads and detecting said bioagents (Claim 1)."

The Miles et al and Casey et al references do not show Applicants' claim limitation, "said potential bioagent particles contain spores and including means for lysis of said spores (Claim 12)."

The Miles et al and Casey et al references do not show Applicants' claim limitation, "said wetted wall sample preparer includes a super serpentine reactor (Claim 19)"

The Miles et al and Casey et al references do not show Applicants' claim limitation, "wherein said flow cytometer for analyzing said optically encoded microbeads with said laser unit includes a red laser that classifies said microbeads and a green laser that quantifies said microbeads (Claim 29)."

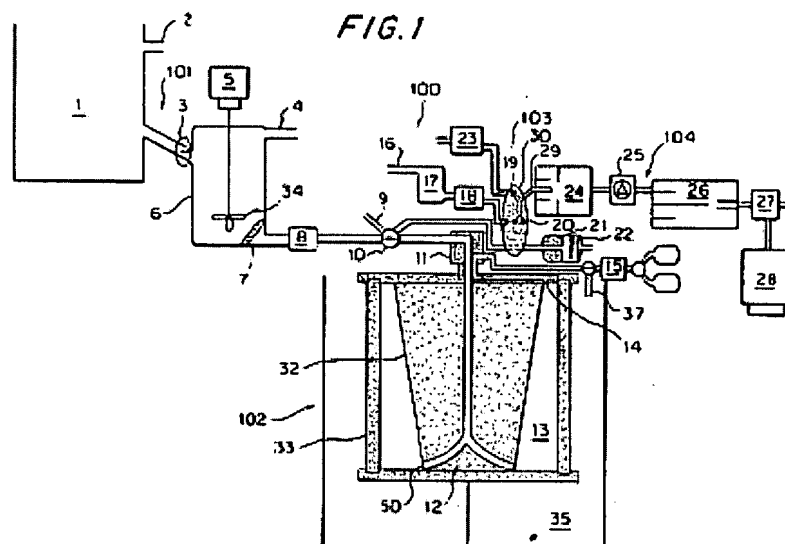
Since Applicants' claim limitations identified above are not shown by the references the Examiner has not factually supported a *prima facie* case of obviousness and the rejection should be withdrawn. Further, the fact that the two references fail to show the limitations identified above, a combination of the two references would produce Applicants' invention.

### 35 U.S.C. §103 Rejection – Wick In View of Casey et al

In numbered paragraphs 18-27 of the Office Action mailed March 27, 2007, claims 1-2, 10, 11, 13-18, 20, 33, and 37-39 were rejected under 35 U.S.C. §103(a) as being unpatentable over the Wick reference (US 6,491,872) in view of the Casey et al reference (US 2002/0187470).

#### The Wick Reference

The Wick reference is United States Patent No. 6,491,872 for detecting and recording submicron sized particles illustrated in figure 1 and the portion of specification of the patent reproduced below.



"A system and method for detecting the presence of submicron sized particles in a sample taken from the environment includes a collecting means for collecting a sample from the environment; and a means for purifying and concentrating the submicron particles in a sample by purifying and concentrating the particles based on size. The purifying and concentrating means includes a means for connecting the collecting means to the purifying and concentrating means for transferring the sample from the collecting means to the means for purifying and concentrating the particles. The system also includes a means for detecting the purified and concentrated particles, wherein the detecting means comprises: an electrospray assembly, the assembly having an electrospray capillary which receives the output from the purifying and concentrating means, a differential mobility analyzer which receives the output from the capillary, and a

condensation particle device for counting the number of particles that pass through the differential mobility analyzer.”

#### The Casey et al Reference

The Casey et al reference is United States Published Patent Application No. 2002/0187470 disclosing methods for rapid detection of single nucleotide polymorphisms (SNPs) in a nucleic acid sample. For example, the Casey et al reference discloses the following method:

“a method of determining a selected nucleotide polymorphism in genomic DNA treated to reduce viscosity comprising (a) performing an amplification of the genomic DNA using a first nucleic acid primer comprising a region complementary to a section of one strand of the nucleic acid that is 5' of the selected nucleotide, and a second nucleic acid primer complimentary to a section of the opposite strand of the nucleic acid downstream of the selected nucleotide, under conditions for specific amplification of the region of the selected nucleotide between the two primers, to form a PCR product; (b) contacting the PCR product with a first nucleic acid linked at its 5' end to a detectably tagged mobile solid support, wherein the first nucleic acid comprises a region complementary to a section of one strand of the PCR product that is directly 5' of and adjacent to the selected nucleotide, under hybridization conditions to form a hybridization product; (c) performing a primer extension reaction with the hybridization product and a detectably labeled, identified chain-terminating nucleotide under conditions for primer extension; (d) detecting the presence or absence of a label incorporated into the hybridization product, the presence of a label indicating the incorporation of the labeled chain-terminating nucleotide into the hybridization product, and the identity of the incorporated labeled chain-terminating nucleotide indicating the identity of the nucleotide complementary to the selected nucleotide; and (e) comparing the identity of the selected nucleotide with a non-polymorphic nucleotide, a different identity of the selected nucleotide from that of the non-polymorphic nucleotide indicating a polymorphism of that selected nucleotide.”

#### Applicants' Response to Rejection Wick In View of Casey et al

Applicants have amended the single independent claim, claim 1; therefore all of the claims presented for examination have effectively been amended.

Applicants believe Applicants believe that amended independent claim 1 and the



dependent rejected claims are patentable and that the Wick and Casey et al references do not support a 35 U.S.C. §103(a) rejection.

The Examiner bears the initial burden of factually supporting a *prima facie* conclusion of obviousness. To establish a *prima facie* case of obviousness, three basic criteria must be met. First, there must be some suggestion or motivation, either in the references themselves or in the knowledge generally available to one of ordinary skill in the art, to modify the reference or to combine reference teachings. Second, there must be a reasonable expectation of success. Finally, the prior art reference (or references when combined) must teach or suggest all the claim limitations. The teaching or suggestion to make the claimed combination and the reasonable expectation of success must both be found in the prior art, and not based on applicant's disclosure. *In re Vaeck*, 947 F.2d 488, 20 USPQ2d 1438 (Fed. Cir. 1991).

#### No Suggestion or Motivation to Combine Wick and Casey et al

The first criteria for supporting a *prima facie* conclusion of obviousness is: there must be some suggestion or motivation, either in the references themselves or in the knowledge generally available to one of ordinary skill in the art, to modify the reference or to combine reference teachings.

There is no suggestion or motivation to combine the Wick detecting and recording submicron sized particles device with the Casey et al methods for rapid detection of single nucleotide polymorphisms in a nucleic acid sample. There is no explanation of how or why the Wick device would or could be combined with the Casey et al methods. Since there is no suggestion or motivation to combine the references Examiner has not factually supported a *prima facie* case of obviousness and the rejection should be withdrawn.

### No Reasonable Expectation of Success

The second criteria for supporting a *prima facie* conclusion of obviousness is there must be a reasonable expectation of success. A combination of the Wick detecting and recording submicron sized particles device with the Casey et al methods for rapid detection of single nucleotide polymorphisms in a nucleic acid sample would not have a reasonable expectation of success. Casey et al shows methods and those methods could not be successfully implemented on the Wick device. Since the combination would not have a reasonable expectation of success the Examiner has not factually supported a *prima facie* case of obviousness and the rejection should be withdrawn.

### References Do Not Teach or Suggest All the Claim Limitations

The Third criteria for supporting a *prima facie* conclusion of obviousness is the prior art reference (or references when combined) must teach or suggest all the claim limitations. In assessing any *prima facie* conclusion of obviousness the guidance of the Supreme Court in *Graham v. John Deere Co.*, 383 U.S. 1, 148 USPQ 459 (1966) is used. *Graham v. John Deere Co.* requires determining “the scope and content of the prior art,” ascertaining “the differences between the prior art and the claims at issue,” and resolving “the level of ordinary skill in the pertinent art.”

There are many differences between the Wick and Casey et al references and Applicants’ claimed invention. For example, Applicants’ claim limitations identified below are missing from the Wick and Casey et al references.

The Wick and Casey et al references do not show Applicants’ claim limitation, “a wetted wall sample preparer for preparing a sample of said selected potential bioagent particles, said wetted wall sample preparer operatively connected to said collector for collecting and preparing said sample from said air gathered by said collector, wherein said wetted wall sample

preparer includes a wetted wall cyclone collector that concentrates said selected potential bioagent particles in a liquid and a unit for adding optically encoded microbeads imbedded with precise ratios of red and orange fluorescent dyes yielding an array of beads having a unique spectral address and each bead coated with capture antibodies specific for a given antigen to said liquid and said selected potential bioagent particles (Claim 1)."

The Wick and Casey et al references do not show Applicants' claim limitation, "a detector for detecting said bioagents in said sample, said detector operatively connected to said wetted wall sample preparer wherein said detector utilizes said optically encoded microbeads and wherein said detector includes a flow cytometer for analyzing said optically encoded microbeads that are imbedded with precise ratios of red and orange fluorescent dyes yielding an array of beads having a unique spectral address and each bead coated with capture antibodies specific for a given antigen with a laser unit for individually interrogating said optically encoded microbeads and detecting said bioagents(Claim 1)."

The Wick and Casey et al references do not show Applicants' claim limitation, "said potential bioagent particles contain spores and including means for lysis of said spores (Claim 12)."

The Wick and Casey et al references do not show Applicants' claim limitation, "said wetted wall sample preparer includes a super serpentine reactor (Claim 19)."

The Wick and Casey et al references do not show Applicants' claim limitation, "wherein said flow cytometer for analyzing said optically encoded microbeads with said laser unit includes a red laser that classifies said microbeads and a green laser that quantifies said microbeads (Claim 29)."

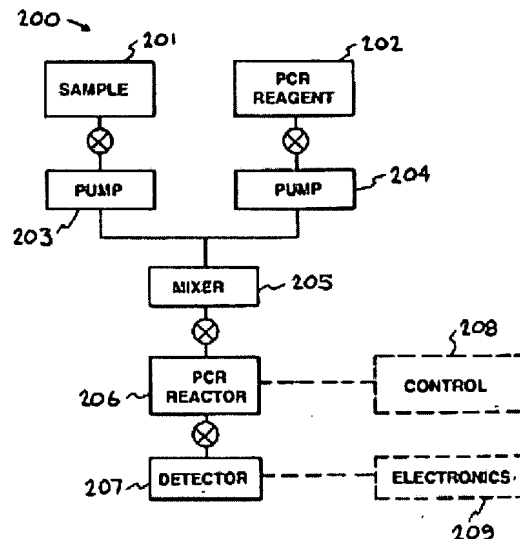
Since Applicants' claim limitations identified above are not shown by the references the Examiner has not factually supported a *prima facie* case of obviousness and the rejection should be withdrawn. Further, the fact that the two references fail to show the limitations identified above, a combination of the two references would produce Applicants' invention.

### 35 U.S.C. §103 Rejection – Colston et al In View of Casey et al

In numbered paragraphs 28-38 of the Office Action mailed March 27, 2007, claims 1, 11, 14-20, 33, and 36-39 were rejected under 35 U.S.C. §103(a) as being unpatentable over the Colston et al reference (US 2003/0032172) in view of the Casey et al reference (US 2002/0187470).

#### The Colston et al Reference

The Colston et al reference is United States Published Patent Application No. 2003/0032172 for an automated nucleic acid assay system illustrated in figure 2 and the portion of specification of the patent reproduced below.



**FIG. 2**

"The system 200 provides a system capable of performing, singly or in combination, sample preparation, nucleic acid amplification, and nucleic acid detection functions. The nucleic acid assay system 200 includes a

number components. A sample is contained in unit 201. A PCR reagent is contained in unit 202. A pump 203 transfers the sample from unit 201 into mixer 205. A pump 204 transfers the PCR reagent from unit 202 into mixer 205. the mixer 205 combines the sample and the PCR reagent. In one embodiment the PCR reagent includes primers. In another embodiment the PCR reagent includes oligos. The mixer 205 can be, for example, a super serpentine reactor, available from Global FIA, Inc, Fox Island, Wash. The mixed sample and reagent are transferred to a PCR reactor 206. This results in an amplified sample. In one embodiment the PCR reactor 206 includes an embedded thermocouple calibration conduit. PCR amplification devices are described in publications such as U.S. Pat. No. 5,589,136 for silicon-based sleeve devices for chemical reactions, assigned to the Regents of the University of California, inventors: M. Allen Northrup, Raymond P. Mariella, Jr., Anthony V. Carrano, and Joseph W. Balch, patented Dec. 31, 1996 and many are commercially available such as ABI PRISM® 7700 Sequence Detection System by Applied Biosystems; iCycler iQ Real-Time PCR Detection System by Bio-Rad; and Smart Cycler® System by Cepheid. The amplified sample is transferred from the PCR reactor 206 detector 207. The detector can be, for example, a detection system described in publications and products produced by Cepheid and Baltimore-based Environmental Technologies Group, Inc. (ETG), a part of London-based Smiths Aerospace.”

#### The Casey et al Reference

The Casey et al reference is United States Published Patent Application No. 2002/0187470 disclosing methods for rapid detection of single nucleotide polymorphisms (SNPs) in a nucleic acid sample. For example, the Casey et al reference discloses the following method:

“a method of determining a selected nucleotide polymorphism in genomic DNA treated to reduce viscosity comprising (a) performing an amplification of the genomic DNA using a first nucleic acid primer comprising a region complementary to a section of one strand of the nucleic acid that is 5' of the selected nucleotide, and a second nucleic acid primer complimentary to a section of the opposite strand of the nucleic acid downstream of the selected nucleotide, under conditions for specific amplification of the region of the selected nucleotide between the two primers, to form a PCR product; (b) contacting the PCR product with a first nucleic acid linked at its 5' end to a detectably tagged mobile solid support, wherein the first nucleic acid comprises a region complementary to a section of one strand of the PCR product that is directly 5' of and adjacent to the selected nucleotide, under hybridization

conditions to form a hybridization product; (c) performing a primer extension reaction with the hybridization product and a detectably labeled, identified chain-terminating nucleotide under conditions for primer extension; (d) detecting the presence or absence of a label incorporated into the hybridization product, the presence of a label indicating the incorporation of the labeled chain-terminating nucleotide into the hybridization product, and the identity of the incorporated labeled chain-terminating nucleotide indicating the identity of the nucleotide complementary to the selected nucleotide; and (e) comparing the identity of the selected nucleotide with a non-polymorphic nucleotide, a different identity of the selected nucleotide from that of the non-polymorphic nucleotide indicating a polymorphism of that selected nucleotide.”

#### **Applicants’ Response to Rejection Colston et al In View of Casey et al**

Applicants have amended the single independent claim, claim 1; therefore all of the claims presented for examination have effectively been amended.

Applicants believe Applicants believe that amended independent claim 1 and the dependent rejected claims are patentable and that the Colston et al and Casey et al references do not support a 35 U.S.C. §103(a) rejection.

The Examiner bears the initial burden of factually supporting a *prima facie* conclusion of obviousness. To establish a *prima facie* case of obviousness, three basic criteria must be met. First, there must be some suggestion or motivation, either in the references themselves or in the knowledge generally available to one of ordinary skill in the art, to modify the reference or to combine reference teachings. Second, there must be a reasonable expectation of success. Finally, the prior art reference (or references when combined) must teach or suggest all the claim limitations. The teaching or suggestion to make the claimed combination and the reasonable expectation of success must both be found in the prior art, and not based on applicant's disclosure. *In re Vaeck*, 947 F.2d 488, 20 USPQ2d 1438 (Fed. Cir. 1991).

#### No Suggestion or Motivation to Combine Colston et al and Casey et al

The first criteria for supporting a *prima facie* conclusion of obviousness is: there must be some suggestion or motivation, either in the references themselves or in the knowledge generally available to one of ordinary skill in the art, to modify the reference or to combine reference teachings.

There is no suggestion or motivation to combine the Colston et al automated nucleic acid assay system with the Casey et al methods for rapid detection of single nucleotide polymorphisms in a nucleic acid sample. There is no explanation of how or why the Colston et al system would or could be combined with the Casey et al methods. Since there is no suggestion or motivation to combine the references Examiner has not factually supported a *prima facie* case of obviousness and the rejection should be withdrawn.

#### No Reasonable Expectation of Success

The second criteria for supporting a *prima facie* conclusion of obviousness is there must be a reasonable expectation of success. A combination of the Colston et al automated nucleic acid assay system with the Casey et al methods for rapid detection of single nucleotide polymorphisms in a nucleic acid sample would not have a reasonable expectation of success. Casey et al shows methods and those methods could not be successfully implemented on the Colston et al device. Since the combination would not have a reasonable expectation of success the Examiner has not factually supported a *prima facie* case of obviousness and the rejection should be withdrawn.

#### References Do Not Teach or Suggest All the Claim Limitations

The Third criteria for supporting a *prima facie* conclusion of obviousness is the prior art reference (or references when combined) must teach or suggest all the claim limitations. In assessing any *prima facie* conclusion of obviousness the guidance of the Supreme Court in *Graham v. John Deere Co.*, 383 U.S. 1, 148 USPQ

459 (1966) is used. *Graham v. John Deere Co.* requires determining “the scope and content of the prior art,” ascertaining “the differences between the prior art and the claims at issue,” and resolving “the level of ordinary skill in the pertinent art.”

There are many differences between the Colston et al and Casey et al references and Applicants’ claimed invention. For example, Applicants’ claim limitations identified below are missing from the Colston et al and Casey et al references.

The Colston et al and Casey et al references do not show Applicants’ claim limitation, “a collector for gathering said air being monitored, said collector separating selected potential bioagent particles from said air (Claim 1).”

The Colston et al and Casey et al references do not show Applicants’ claim limitation, “a wetted wall sample preparer for preparing a sample of said selected potential bioagent particles, said wetted wall sample preparer operatively connected to said collector for collecting and preparing said sample from said air gathered by said collector, wherein said wetted wall sample preparer includes a wetted wall cyclone collector that concentrates said selected potential bioagent particles in a liquid and a unit for adding optically encoded microbeads imbedded with precise ratios of red and orange fluorescent dyes yielding an array of beads having a unique spectral address and each bead coated with capture antibodies specific for a given antigen to said liquid and said selected potential bioagent particles (Claim 1).”

The Colston et al and Casey et al references do not show Applicants’ claim limitation, “a detector for detecting said bioagents in said sample, said detector operatively connected to said wetted wall sample preparer wherein said detector utilizes said optically encoded microbeads and wherein said detector includes a flow cytometer for analyzing said optically encoded microbeads that are



imbedded with precise ratios of red and orange fluorescent dyes yielding an array of beads having a unique spectral address and each bead coated with capture antibodies specific for a given antigen with a laser unit for individually interrogating said optically encoded microbeads and detecting said bioagents(Claim 1)."

The Colston et al and Casey et al references do not show Applicants' claim limitation, "said potential bioagent particles contain spores and including means for lysis of said spores (Claim 12)."

The Colston et al and Casey et al references do not show Applicants' claim limitation, "said wetted wall sample preparer includes a super serpentine reactor (Claim 19)"

The Colston et al and Casey et al references do not show Applicants' claim limitation, "wherein said flow cytometer for analyzing said optically encoded microbeads with said laser unit includes a red laser that classifies said microbeads and a green laser that quantifies said microbeads (Claim 29)."

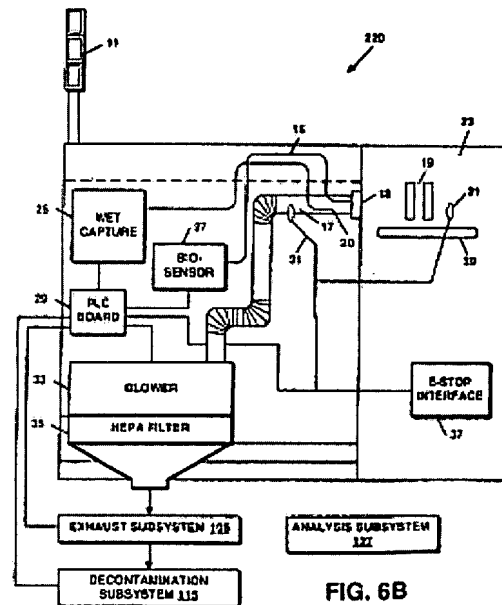
Since Applicants' claim limitations identified above are not shown by the references the Examiner has not factually supported a *prima facie* case of obviousness and the rejection should be withdrawn. Further, the fact that the two references fail to show the limitations identified above, a combination of the two references would produce Applicants' invention.

### **35 U.S.C. §103 Rejection – Daugherty et al In View of Casey et al**

In numbered paragraphs 39-48 of the Office Action mailed March 27, 2007, claims 1-5, 7, 9-11, 32, 33, and 35-37 were rejected under 35 U.S.C. §103(a) as being unpatentable over the Daugherty et al reference (US 2004/0028561) in view of the Casey et al reference (US 2002/0187470).

## The Daugherty et al Reference

The Daugherty et al reference is United States Published Patent Application No. 2004/0028561 for a system for the detection of pathogens in the mail stream illustrated in figure 6B and the portion of specification of the patent reproduced below.



"Referring now to FIGS. 6A and 6B, system 220, in which the illustrative embodiment of the control flow 220 for mail sortation is shown. As mail pieces are fed into system 220, through feeder 41, particles are released through normal handling and/or through pinch point pulley assembly 19. Particles are moved through prefilter 18 which allows large particles to pass through the prefilter 18 and exhaust back into the blower/air filtration system 33/35 through simplified hoodless ducting 17 as waste air. Smaller particles enter pitot tube entry 20, into the region in which the particles are tested for contamination. In the illustrative embodiment, the region includes sampling subsystem 123 and triggering subsystem 119 (shown in FIG. 1), embodied in wet capture 25 and biosensor 27/indicator light 11 respectively. After the mail parcels have been fed into the system, they proceed through closed vent/hood 23 on mail transport device 39 towards mail stacker 43 which is enclosed by open vent/hood 45. In general, conventional closed and open vent/hoods 23 and 45, respectively, are custom-fitted to all types of mail transport equipment (i.e. mail transport equipment manufactured by Lockheed Martin, Pitney-Bowes, Bell & Howell, Siemens, etc.) and conventional mail sortation stacker sections 43, pockets, or sort bin

destinations typically installed at mail processing facilities as well as commercial pre-sort facilities and mailrooms.”

### The Casey et al Reference

The Casey et al reference is United States Published Patent Application No. 2002/0187470 disclosing methods for rapid detection of single nucleotide polymorphisms (SNPs) in a nucleic acid sample. For example, the Casey et al reference discloses the following method:

“a method of determining a selected nucleotide polymorphism in genomic DNA treated to reduce viscosity comprising (a) performing an amplification of the genomic DNA using a first nucleic acid primer comprising a region complementary to a section of one strand of the nucleic acid that is 5' of the selected nucleotide, and a second nucleic acid primer complimentary to a section of the opposite strand of the nucleic acid downstream of the selected nucleotide, under conditions for specific amplification of the region of the selected nucleotide between the two primers, to form a PCR product; (b) contacting the PCR product with a first nucleic acid linked at its 5' end to a detectably tagged mobile solid support, wherein the first nucleic acid comprises a region complementary to a section of one strand of the PCR product that is directly 5' of and adjacent to the selected nucleotide, under hybridization conditions to form a hybridization product; (c) performing a primer extension reaction with the hybridization product and a detectably labeled, identified chain-terminating nucleotide under conditions for primer extension; (d) detecting the presence or absence of a label incorporated into the hybridization product, the presence of a label indicating the incorporation of the labeled chain-terminating nucleotide into the hybridization product, and the identity of the incorporated labeled chain-terminating nucleotide indicating the identity of the nucleotide complementary to the selected nucleotide; and (e) comparing the identity of the selected nucleotide with a non-polymorphic nucleotide, a different identity of the selected nucleotide from that of the non-polymorphic nucleotide indicating a polymorphism of that selected nucleotide.”

### Applicants' Response - Rejection Daugherty et al In View of Casey et al

Applicants have amended the single independent claim, claim 1; therefore all of the claims presented for examination have effectively been amended.

Applicants believe Applicants believe that amended independent claim 1 and the

dependent rejected claims are patentable and that the Daugherty et al and Casey et al references do not support a 35 U.S.C. §103(a) rejection.

The Examiner bears the initial burden of factually supporting a *prima facie* conclusion of obviousness. To establish a *prima facie* case of obviousness, three basic criteria must be met. First, there must be some suggestion or motivation, either in the references themselves or in the knowledge generally available to one of ordinary skill in the art, to modify the reference or to combine reference teachings. Second, there must be a reasonable expectation of success. Finally, the prior art reference (or references when combined) must teach or suggest all the claim limitations. The teaching or suggestion to make the claimed combination and the reasonable expectation of success must both be found in the prior art, and not based on applicant's disclosure. *In re Vaeck*, 947 F.2d 488, 20 USPQ2d 1438 (Fed. Cir. 1991).

No Suggestion or Motivation to Combine Daugherty et al and Casey et al

The first criteria for supporting a *prima facie* conclusion of obviousness is: there must be some suggestion or motivation, either in the references themselves or in the knowledge generally available to one of ordinary skill in the art, to modify the reference or to combine reference teachings.

There is no suggestion or motivation to combine the Daugherty et al system for the detection of pathogens in the mail stream with the Casey et al methods for rapid detection of single nucleotide polymorphisms in a nucleic acid sample. There is no explanation of how or why the Daugherty et al system would or could be combined with the Casey et al methods. Since there is no suggestion or motivation to combine the references Examiner has not factually supported a *prima facie* case of obviousness and the rejection should be withdrawn.

### No Reasonable Expectation of Success

The second criteria for supporting a *prima facie* conclusion of obviousness is there must be a reasonable expectation of success. A combination of the Daugherty et al system for the detection of pathogens in the mail stream with the Casey et al methods for rapid detection of single nucleotide polymorphisms in a nucleic acid sample would not have a reasonable expectation of success. Casey et al shows methods and those methods could not be successfully implemented on the Daugherty et al device. Since the combination would not have a reasonable expectation of success the Examiner has not factually supported a *prima facie* case of obviousness and the rejection should be withdrawn.

### References Do Not Teach or Suggest All the Claim Limitations

The Third criteria for supporting a *prima facie* conclusion of obviousness is the prior art reference (or references when combined) must teach or suggest all the claim limitations. In assessing any *prima facie* conclusion of obviousness the guidance of the Supreme Court in *Graham v. John Deere Co.*, 383 U.S. 1, 148 USPQ 459 (1966) is used. *Graham v. John Deere Co.* requires determining “the scope and content of the prior art,” ascertaining “the differences between the prior art and the claims at issue,” and resolving “the level of ordinary skill in the pertinent art.”

There are many differences between the Daugherty et al and Casey et al references and Applicants’ claimed invention. For example, Applicants’ claim limitations identified below are missing from the Daugherty et al and Casey et al references.

The Daugherty et al and Casey et al references do not show Applicants’ claim limitation, “a collector for gathering said air being monitored, said collector separating selected potential bioagent particles from said air (Claim 1).”

The Daugherty et al and Casey et al references do not show Applicants' claim limitation, "a wetted wall sample preparer for preparing a sample of said selected potential bioagent particles, said wetted wall sample preparer operatively connected to said collector for collecting and preparing said sample from said air gathered by said collector, wherein said wetted wall sample preparer includes a wetted wall cyclone collector that concentrates said selected potential bioagent particles in a liquid and a unit for adding optically encoded microbeads imbedded with precise ratios of red and orange fluorescent dyes yielding an array of beads having a unique spectral address and each bead coated with capture antibodies specific for a given antigen to said liquid and said selected potential bioagent particles (Claim 1)."

The Daugherty et al and Casey et al references do not show Applicants' claim limitation, "a detector for detecting said bioagents in said sample, said detector operatively connected to said wetted wall sample preparer wherein said detector utilizes said optically encoded microbeads and wherein said detector includes a flow cytometer for analyzing said optically encoded microbeads that are imbedded with precise ratios of red and orange fluorescent dyes yielding an array of beads having a unique spectral address and each bead coated with capture antibodies specific for a given antigen with a laser unit for individually interrogating said optically encoded microbeads and detecting said bioagents(Claim 1)."

The Daugherty et al and Casey et al references do not show Applicants' claim limitation, "said potential bioagent particles contain spores and including means for lysis of said spores (Claim 12)."

The Daugherty et al and Casey et al references do not show Applicants' claim limitation, "said wetted wall sample preparer includes a super serpentine reactor (Claim 19)"

The Daugherty et al and Casey et al references do not show Applicants' claim limitation, "wherein said flow cytometer for analyzing said optically encoded microbeads with said laser unit includes a red laser that classifies said microbeads and a green laser that quantifies said microbeads (Claim 29)."

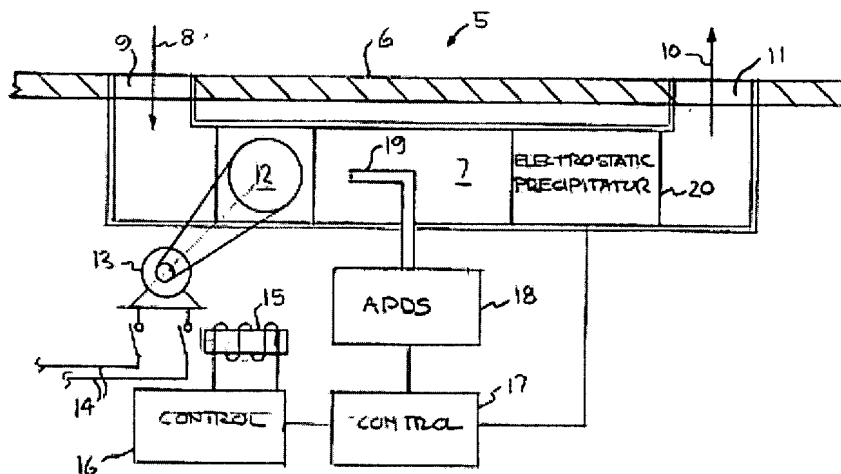
Since Applicants' claim limitations identified above are not shown by the references the Examiner has not factually supported a *prima facie* case of obviousness and the rejections should be withdrawn. Further, the fact that the two references fail to show the limitations identified above, a combination of the two references would produce Applicants' invention.

#### **35 U.S.C. §103 Rejection – Mariella In View of Casey et al**

In numbered paragraphs 50-58 of the Office Action mailed March 27, 2007, claims 1-3, 8-11, 30, and 40 were rejected under 35 U.S.C. §103(a) as being unpatentable over the Mariella reference (US 6,787,104) in view of the Casey et al reference (US 2002/0187470).

#### **The Mariella Reference**

The Mariella reference is United States Patent No. 6,787,104 for a system for detection and treatment of chemical weapons and/or biological pathogens illustrated in figure 2 and the portion of specification of the patent reproduced below.



**FIG. 2**

"A continuous sample of the air stream is channeled to APDS 18 through conduit 19. The APDS 18 is located within the air stream for detecting the unwanted agents. The APDS 18 is connected to an electrostatic precipitator/scrubber 21. The electrostatic precipitator/scrubber 21 can be a system that traps the airborne threat using electrostatic precipitation. The electrostatic precipitator/scrubber 21 can be a system that uses an aqueous-based spray/aerosol scrubbing system. Alternatively, the electrostatic precipitator/scrubber 21 can be a system that uses both electrostatic precipitation and an aqueous-based spray/aerosol scrubbing system. Upon detection of an unwanted agent the autonomous chemical and pathogen detector 18 provides a signal to electrostatic precipitator/scrubber 21. The precipitator/scrubber coils 20 inside of air duct are energized to treat the chemical or biological agent."

### The Casey et al Reference

The Casey et al reference is United States Published Patent Application No. 2002/0187470 disclosing methods for rapid detection of single nucleotide polymorphisms (SNPs) in a nucleic acid sample. For example, the Casey et al reference discloses the following method:

"a method of determining a selected nucleotide polymorphism in genomic DNA treated to reduce viscosity comprising (a) performing an amplification of the genomic DNA using a first nucleic acid primer comprising a region complementary to a section of one strand of the nucleic acid that is 5' of the selected nucleotide, and a second nucleic acid primer complimentary to a section of the opposite strand of the nucleic acid downstream of the selected nucleotide, under conditions for specific amplification of the region of the



selected nucleotide between the two primers, to form a PCR product; (b) contacting the PCR product with a first nucleic acid linked at its 5' end to a detectably tagged mobile solid support, wherein the first nucleic acid comprises a region complementary to a section of one strand of the PCR product that is directly 5' of and adjacent to the selected nucleotide, under hybridization conditions to form a hybridization product; (c) performing a primer extension reaction with the hybridization product and a detectably labeled, identified chain-terminating nucleotide under conditions for primer extension; (d) detecting the presence or absence of a label incorporated into the hybridization product, the presence of a label indicating the incorporation of the labeled chain-terminating nucleotide into the hybridization product, and the identity of the incorporated labeled chain-terminating nucleotide indicating the identity of the nucleotide complementary to the selected nucleotide; and (e) comparing the identity of the selected nucleotide with a non-polymorphic nucleotide, a different identity of the selected nucleotide from that of the non-polymorphic nucleotide indicating a polymorphism of that selected nucleotide."

#### **Applicants' Response to Rejection Mariella In View of Casey et al**

Applicants have amended the single independent claim, claim 1; therefore all of the claims presented for examination have effectively been amended. Applicants believe Applicants believe that amended independent claim 1 and the dependent rejected claims are patentable and that the Mariella and Casey et al references do not support a 35 U.S.C. §103(a) rejection.

The Examiner bears the initial burden of factually supporting a *prima facie* conclusion of obviousness. To establish a *prima facie* case of obviousness, three basic criteria must be met. First, there must be some suggestion or motivation, either in the references themselves or in the knowledge generally available to one of ordinary skill in the art, to modify the reference or to combine reference teachings. Second, there must be a reasonable expectation of success. Finally, the prior art reference (or references when combined) must teach or suggest all the claim limitations. The teaching or suggestion to make the claimed combination and the reasonable expectation of success must both be found in the prior art,

and not based on applicant's disclosure. *In re Vaeck*, 947 F.2d 488, 20 USPQ2d 1438 (Fed. Cir. 1991).

No Suggestion or Motivation to Combine Mariella and Casey et al

The first criteria for supporting a *prima facie* conclusion of obviousness is: there must be some suggestion or motivation, either in the references themselves or in the knowledge generally available to one of ordinary skill in the art, to modify the reference or to combine reference teachings.

There is no suggestion or motivation to combine the Mariella system for detection and treatment of chemical weapons and/or biological pathogens with the Casey et al methods for rapid detection of single nucleotide polymorphisms in a nucleic acid sample. There is no explanation of how or why the Mariella system would or could be combined with the Casey et al methods. Since there is no suggestion or motivation to combine the references Examiner has not factually supported a *prima facie* case of obviousness and the rejection should be withdrawn.

No Reasonable Expectation of Success

The second criteria for supporting a *prima facie* conclusion of obviousness is there must be a reasonable expectation of success. A combination of the Mariella system for detection and treatment of chemical weapons and/or biological pathogens with the Casey et al methods for rapid detection of single nucleotide polymorphisms in a nucleic acid sample would not have a reasonable expectation of success. Casey et al shows methods and those methods could not be successfully implemented on the Mariella device. Since the combination would not have a reasonable expectation of success the Examiner has not factually supported a *prima facie* case of obviousness and the rejection should be withdrawn.

### References Do Not Teach or Suggest All the Claim Limitations

The Third criteria for supporting a *prima facie* conclusion of obviousness is the prior art reference (or references when combined) must teach or suggest all the claim limitations. In assessing any *prima facie* conclusion of obviousness the guidance of the Supreme Court in *Graham v. John Deere Co.*, 383 U.S. 1, 148 USPQ 459 (1966) is used. *Graham v. John Deere Co.* requires determining “the scope and content of the prior art,” ascertaining “the differences between the prior art and the claims at issue,” and resolving “the level of ordinary skill in the pertinent art.”

There are many differences between the Mariella and Casey et al references and Applicants’ claimed invention. For example, Applicants’ claim limitations identified below are missing from the Mariella and Casey et al references.

The Mariella and Casey et al references do not show Applicants’ claim limitation, “a collector for gathering said air being monitored, said collector separating selected potential bioagent particles from said air (Claim 1).”

The Mariella and Casey et al references do not show Applicants’ claim limitation, “a wetted wall sample preparer for preparing a sample of said selected potential bioagent particles, said wetted wall sample preparer operatively connected to said collector for collecting and preparing said sample from said air gathered by said collector, wherein said wetted wall sample preparer includes a wetted wall cyclone collector that concentrates said selected potential bioagent particles in a liquid and a unit for adding optically encoded microbeads imbedded with precise ratios of red and orange fluorescent dyes yielding an array of beads having a unique spectral address and each bead coated with capture antibodies specific for a given antigen to said liquid and said selected potential bioagent particles (Claim 1).”

The Mariella and Casey et al references do not show Applicants' claim limitation, "a detector for detecting said bioagents in said sample, said detector operatively connected to said wetted wall sample preparer wherein said detector utilizes said optically encoded microbeads and wherein said detector includes a flow cytometer for analyzing said optically encoded microbeads that are imbedded with precise ratios of red and orange fluorescent dyes yielding an array of beads having a unique spectral address and each bead coated with capture antibodies specific for a given antigen with a laser unit for individually interrogating said optically encoded microbeads and detecting said bioagents(Claim 1)."

The Mariella and Casey et al references do not show Applicants' claim limitation, "said potential bioagent particles contain spores and including means for lysis of said spores (Claim 12)."

The Mariella and Casey et al references do not show Applicants' claim limitation, "said wetted wall sample preparer includes a super serpentine reactor (Claim 19)"

The Mariella and Casey et al references do not show Applicants' claim limitation, "wherein said flow cytometer for analyzing said optically encoded microbeads with said laser unit includes a red laser that classifies said microbeads and a green laser that quantifies said microbeads (Claim 29)."

Since Applicants' claim limitations identified above are not shown by the references the Examiner has not factually supported a *prima facie* case of obviousness and the rejections should be withdrawn. Further, the fact that the two references fail to show the limitations identified above, a combination of the two references would produce Applicants' invention.


**Rejection – Daugherty et al, Casey et al, and Lawless et al**

In numbered paragraph 59 of the Office Action mailed March 27, 2007, claims 1-5, 7, 9-11, 32, 33, and 35-37 were rejected under 35 U.S.C. §103(a) as being unpatentable over the Daugherty et al reference (US 2004/0028561) in view of the Casey et al reference (US 2002/0187470) in view of the Lawless et al reference (US 4,923,491). Claim 6 has been cancelled.

**SUMMARY**

The undersigned respectfully submits that, in view of the foregoing amendments and the foregoing remarks, the rejections of the claims raised in the Office Action dated March 27, 2007 have been fully addressed and overcome, and the present application is believed to be in condition for allowance. It is respectfully requested that this application be reconsidered, that the claims be allowed, and that this case be passed to issue. If it is believed that a telephone conversation would expedite the prosecution of the present application, or clarify matters with regard to its allowance, the Examiner is invited to call the undersigned attorney at (925) 424-6897.

Respectfully submitted,



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Dated: May 29, 2007